

You have missed cancer: the unwanted plot twist of benign surgeries

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ABSTRACT

Aims: Surgical interventions for benign conditions are frequently performed in general surgery practice; however, the incidental detection of malignancies in these specimens represents a clinically significant and often overlooked issue. This study aimed to investigate the incidence, pathological characteristics, and follow-up status of incidental malignancies identified in routinely resected specimens, with a particular emphasis on the adequacy of postoperative notification and follow-up processes.

Methods: A retrospective cohort study was conducted on 2.590 surgical procedures—appendectomy, cholecystectomy, abdominal wall hernia repair, hemorrhoidectomy, and pilonidal sinus excision—performed between January 1, 2023, and January 1, 2024, at a tertiary care institution. Patients with preoperatively known or radiologically suspected malignancies were excluded. Pathological reports were reviewed for incidental malignant findings, and follow-up data were obtained via electronic health records and direct patient communication.

Results: Among the reviewed cases, ten incidental malignancies (0.39%) were identified: eight in appendectomy specimens, one in a cholecystectomy specimen, and one in a hernia sac. Remarkably, 30% of the affected patients were unaware of their pathological diagnosis until they were contacted by the researchers. Significant variability in specimen submission practices, especially in hernia and hemorrhoidectomy cases, may have contributed to underdiagnosis.

Conclusion: Although rare, incidental malignancies carry substantial prognostic implications if left unrecognized or inadequately managed. Routine pathological evaluation of all surgical specimens—regardless of presumed benignity—and the implementation of automated alert systems for critical pathology results are essential for timely diagnosis, appropriate referral, and improved patient outcomes.

Keywords: Incidental malignancy, surgical pathology, appendectomy, cholecystectomy, follow-up systems

INTRODUCTION

Surgeons routinely perform procedures for both benign and malignant conditions. In malignant cases, both surgical intervention and pathological assessment are of critical oncological importance. Preoperative planning typically depends on the identification of malignancy, as revealed by clinical evaluations and diagnostic imaging. Surgeons provide relevant clinical information to pathologists, reflecting these preoperative assessments. Patients then rely on their physicians to interpret the pathology results and determine the course of treatment. This sequence represents the standard clinical workflow.

However, missed malignancy cases pose a significant challenge for clinicians, pathologists, and patients. These cases occur when malignancy is not suspected preoperatively due to the absence of clinical or radiological evidence. As a result, surgeons may not provide pathologists with any indication of potential malignancy. In some instances, specimens may not even be sent for pathological evaluation. Pathologists typically perform macroscopic examinations of submitted specimens

and, based on their expertise, may proceed with microscopic evaluation if deemed necessary. Following this, a pathological report is issued.

Although the incidence of such cases is low, a single missed malignancy can have serious consequences for the patient. Delayed diagnosis and treatment may lead to disease progression and significantly worsen prognosis. These concerns highlight the need for systematic pathological evaluation, even in specimens from surgeries generally considered benign.

Some surgical procedures (appendectomy, abdominal wall hernia repair, cholecystectomy, and hemorrhoidectomy) are predominantly performed for benign conditions. However, incidental malignancies are occasionally detected on pathology of specimens from these procedures. The incidence of incidental malignancy has been reported in the published literature as 0.13%, 0.7%, 0.59%, 0.78%, and 0% in hemorrhoidectomy, post-cholecystectomy gallbladder,

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hernia sac, appendectomy, and pilonidal sinus specimens, respectively.¹⁻⁵ The flag at this stage: Do patients get back to their pathological report? The question is whether surgeons should be responsible for ensuring appropriate follow-up. What role do pathologists play in such cases? This study aims to address these questions, specifically the management of and outcomes for incidental malignancies.

The primary objective of this study is not to reassess the incidence rates of incidental malignancies. Instead, we aim to: Investigate the clinical outcomes and management of incidental malignancies detected during routine pathological examinations and identify strategies to minimize missed malignancies and improve patient outcomes.

METHODS

Ethics

The study protocol was reviewed and approved by Hitit University Non-interventional Clinical Researches Ethics Committee (Date: 15.10.2024, Decision No: 2024-107). Due to the retrospective nature of the study and use of de-identified patient data, the requirement for informed consent was waived. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Patient Selection

This study analyzed 2,590 surgical procedures performed on 2,526 patients aged 18 to 85 years. The included procedures were appendectomy, cholecystectomy, abdominal wall hernia repair, hemorrhoidectomy, and pilonidal sinus surgery. Patients were included in the study if they met the following criteria: age between 18 and 85 years and availability of complete clinical and pathological data for analysis.

Strict exclusion criteria were applied to enhance the reliability of the findings. Patients were excluded if they had known malignancies preoperatively or radiological evidence of tumors in the target organ. Additional exclusions included patients with congenital or chronic diseases unrelated to the surgical indication, autoimmune disorders, or incomplete medical records.

Data Collection and Processing

Clinical data were retrieved from the hospital's electronic records. For cases where follow-up details were not documented, patients or their families were contacted directly to obtain the required information. Surgical specimens were submitted for pathological analysis where indicated. Data on patient demographics, surgical details, pathological diagnoses, and timelines for pathology reporting and patient notification were recorded and analyzed.

The necessary institutional permissions were obtained prior to the initiation of data collection and analysis. Patient confidentiality was ensured by anonymizing all data. Informed consent was not required as this study was based on retrospective analysis of medical records without direct patient involvement.

Specimen Submission Practices

All specimens obtained during appendectomy, cholecystectomy, and pilonidal sinus surgeries were submitted for pathological examination. In contrast, 19.4% of hemorrhoidectomy specimens and 68.3% of hernia sacs were not submitted, reflecting variability in surgical practice. Reasons for non-submission were noted and analyzed to evaluate the impact of such practices on diagnostic outcomes.

This version integrates the ethical information seamlessly into the main text without requiring a separate heading, ensuring it adheres to the conventions of an original article.

RESULTS

There were 2526 patients who have including and excluding criteria. But some of them underwent to surgery more than one. So we examined 2590 operation. If the patient who had pathological malignancy or radiological tumor in the organ that is target for the operation didn't include to study. But if the patient had a irrelevant or old malignancy from the applied operation included to study.

Among the procedures performed, 438 patients underwent open appendectomy and 65 underwent laparoscopic appendectomy. For cholecystectomy, 40 were open and 718 were laparoscopic. Additionally, 132 patients underwent pilonidal sinus excision. All specimens from appendectomy, cholecystectomy, and pilonidal sinus surgeries were submitted for pathological evaluation by the surgeons.

Hemorrhoidectomy was performed in 72 patients, of which 58 specimens (80.6%) were submitted for pathological analysis. This indicates that 19.4% of hemorrhoidectomy specimens were not evaluated histologically.

A total of 1,122 patients underwent surgery for abdominal wall hernias via open or laparoscopic techniques. However, only 356 specimens (31.7%) were sent for pathological examination in these cases.

A total of 10 patients pathology results are reported as malign. Only one patient had hernia surgery and one patient had cholecystectomy. The other eight patients underwent appendectomy as emergency procedures. Patients or their family members were contacted to obtain detailed follow-up information when the hospital's electronic records were incomplete.

Case-Specific Findings Cholecystectomy Cases

This patient presented with acute abdomen due to a perforated gallbladder during hospitalization. During surgery, the surgeon observed a tumoral gallbladder and requested an intraoperative frozen section analysis. The pathological examination revealed a 7 cm adenocarcinoma of the gallbladder. Despite surgical intervention, the patient passed away on the 35th day of hospitalization due to comorbidities and a deteriorated general condition (**Table**).

Umbilical Hernia Cases

This patient underwent emergency surgery for an incarcerated umbilical hernia. Preoperative computed tomography (CT) imaging revealed liver lesions consistent with metastasis.

Table. Patients with incidental malignant cancer and their characteristics

Procedure	Total cases	Malignancy detected (n)	Rate (%)
Appendectomy	1.022	8	0.78
Cholecystectomy	812	1	0.12
Hernia repair	496	1	0.20
Hemorrhoidectomy	154	0	0.00
Pilonidal sinus	106	0	0.00
Total	2.590	10	0.39

During surgery, a biopsy of the omentum was performed. Postoperative pathology confirmed omental metastasis of adenocarcinoma. Subsequent investigations, including colonoscopy, identified the primary tumor in the colon (Table).

Appendectomy Cases

Of the eight patients with malignancies identified in appendectomy specimens:

- Suspicion of malignancy was raised peroperatively in only one case, and the patient was informed about the critical importance of the pathological findings.
- Two patients underwent salvage surgery at other healthcare centers following the initial diagnosis.
- Three patients continued follow-up care under the supervision of an oncologist.
- Three patients did not follow up on their pathology results and were unaware of their malignancies until they were contacted during this study. Two of these patients were found to reside in different cities, complicating follow-up (Table).

DISCUSSION

Appendectomy is a surgery commonly performed in a general surgery setting as an emergency procedure. The most common indication for appendectomy is acute appendicitis, and appendiceal malignancies are exceedingly rare in the preoperative diagnosis. Most appendiceal neoplasms are discovered incidentally in pathology reports after appendectomy for presumed acute appendicitis. Nevertheless, their incidence rate is low. The incidence of primary appendiceal cancer in the United States is estimated to be approximately 1–2 cases per 100,000 individuals per year.⁶

In a systematic review and meta-analysis conducted by Bastiaenen et al.,⁷ the incidence of appendiceal neoplasms was reported to be approximately 0.71%, including neuroendocrine tumors (0.35%), non-invasive epithelial tumors (0.15%), and invasive tumors (0.01%). Similarly, a meta-analysis of 25 studies identified neoplasms in 0.71% of appendectomy specimens, comprising neuroendocrine tumors at 0.35%, non-invasive epithelial tumors at 0.15%, and invasive tumors at 0.01%.⁸

Malignancies originating from hernia sacs are exceedingly rare, with an incidence reported to be less than 1% in most studies. Certain neoplasms identified in hernia sac tissue

specimens may be associated with a history of primary malignancies in the patient.^{3,8,9} The routine pathological examination of all hernia sacs remains a subject of ongoing debate. While some authors and professional societies advocate for such examinations due to the possibility of detecting rare malignancies, others oppose this practice.

Hemorrhoidectomy is a frequently performed surgical procedure for managing hemorrhoidal disease, and pathological examination of excised specimens can occasionally uncover unexpected findings such as infectious diseases, dysplasia, or malignancies. Systematic reviews indicate that dysplasia or neoplasia is present in approximately 1.16% of cases, whereas malignancies are far less common, with an incidence ranging from 0.13% to 0.4%.¹⁰ The low prevalence of malignancy has led many clinicians to forgo routine pathological examination of hemorrhoidectomy specimens. Nevertheless, studies such as that by Sakata et al.¹ highlight the potential value of such examinations, as early-stage anal squamous cell carcinoma (ASCC) has been detected in hemorrhoid specimens, underscoring the importance of vigilant pathological assessment.

Pilonidal sinus disease, while not life-threatening, can be recurrent and sometimes necessitates surgical excision. Histopathological findings in these cases predominantly reveal chronic inflammation, with malignancy being exceedingly rare. For example, Alarcón-Del Agua et al.³ reported only 4 cases of carcinoma among 3,729 pilonidal disease specimens. Additionally, a comprehensive review by Safadi et al.⁴ encompassing 103 studies conducted over a century identified 140 cases of squamous cell carcinoma associated with pilonidal disease, with a recurrence rate of 46.6% in patients undergoing follow-up. Gallbladder cancer (GBC) is the most common biliary tract malignancy.⁴ Incidental gallbladder cancer (IGBC), diagnosed intraoperatively or via pathology, is rare and often requires radical resection unless detected at an early stage.³ A meta-analysis by Choi et al.⁹ reported an IGBC incidence of 0.7% among patients undergoing cholecystectomy for benign gallbladder disease.

The existing literature predominantly focuses on abnormal findings, malignancy rates, prognosis, and management of malignancies. However, follow-up rates for abnormal pathology results are less frequently discussed. Jones et al.⁵ reported follow-up rates of 65.1% at three months and 84.8% at one year for patients with abnormal gynecologic cytology, with higher follow-up rates for malignancies (75.9% and 85.6%, respectively). Notably, younger patients (<30 years old) were less likely to follow up. The College of Physicians and Surgeons of Saskatchewan emphasizes the clinician's responsibility in following up on critical and malignant pathology results.¹¹

Despite advancements in diagnostic methods, incidental neoplasms often go undetected prior to surgery. One of the most cited reasons in the literature is the absence of symptoms or the presence of only subclinical signs. For example, adrenal masses—commonly referred to as “incidentalomas”—are predominantly non-functioning benign adrenocortical adenomas, which account for approximately 89.7% of all such lesions.¹² In a review of 87,065 autopsies from 25 studies,

Young et al.¹³ found that 6% of individuals had benign adrenal adenomas, most of which were associated with subclinical Cushing's syndrome. This phenomenon is not exclusive to adrenal tumors and can extend to other organ systems as well.

In the preoperative evaluation process, serological tests are commonly performed. These are minimally invasive and suitable for use in primary care settings. However, many neoplasms do not manifest abnormalities in routine laboratory tests, particularly in the early stages.^{14,15} Because such tumors are often subclinical and do not prompt disease-specific investigations, opportunities for early detection may be missed.¹⁶

Radiological imaging is typically employed in the second stage of preoperative assessment. Nevertheless, in some cases, imaging is not performed due to factors such as high cost, concerns about nephrotoxicity from contrast agents, or contraindications such as allergy.¹²

Even when radiological imaging is performed, interpretation errors may still occur, often influenced by the radiologist's level of expertise, attentiveness, and adherence to systematic review protocols. Diagnostic error rates in radiology range from 3.6% to 16.1%, with an average of 7.6%.¹⁷ Common pitfalls include perceptual errors, premature satisfaction after identifying the first abnormality ("satisfaction of search"), failure to assess anatomical blind spots, and an overreliance on pattern recognition. In addition to human factors, technical limitations such as inadequate contrast enhancement, poor bowel opacification, patient movement, and suboptimal scanning protocols also contribute to missed lesions. Frequently overlooked anatomical regions include the supraclavicular and paraspinal areas, soft tissue compartments, and osseous structures.¹⁷

Additional interpretive challenges may arise from postoperative changes, anatomical variants, or artifacts such as surgical scarring and prior trauma. These may superimpose over lesions or mimic normal anatomy, complicating the identification of neoplastic processes. Multidetector computed tomography (MDCT), especially in trauma settings, has been shown to have diagnostic blind spots, false negatives, and artifact-related pitfalls.¹⁸

Ultimately, the absence of standardized preoperative imaging protocols for benign surgical conditions creates a diagnostic gap. Neoplasms that could have been detected radiologically often remain unnoticed until a histopathological review is conducted postoperatively.

The malignancy rate in our study for specimens obtained from surgeries performed for benign diseases was less than 1%. This exceptionally low rate likely contributes to a less vigilant approach by both patients and clinicians toward pathology reports. Unexpected malignant findings in such cases may even surprise the diagnosticians. Within hospital systems, critical laboratory results are typically flagged to ensure timely notification of clinicians. Adopting a similar strategy for pathology reports by introducing a "critical findings alert" for unexpected malignant results could significantly enhance

follow-up rates. This approach would enable timely clinical interventions, ultimately improving patient outcomes.

Limitations

Among the strengths of this study is that it addresses an often-overlooked issue with a comprehensive, real-world dataset covering various routine surgeries. However, several limitations must be acknowledged. First, the retrospective design inherently limits the ability to assess causality and may miss undocumented clinical outcomes. Second, the study was conducted at a single tertiary care center, which may affect the generalizability of the findings. Third, follow-up data were partially dependent on patient recall and contactability, which introduces the possibility of information bias. Additionally, pathology submission practices varied between procedures and were not standardized, potentially leading to underreporting of incidental malignancies. Despite these limitations, the study underscores the need for systematized pathological evaluation and follow-up processes in general surgery.

CONCLUSION

Patients undergoing surgery for benign conditions often neglect to follow up on pathology results due to the low perceived risk of malignancy. Similarly, clinicians, overwhelmed by demanding workloads, may inadvertently overlook such findings. Together, these factors heighten the risk of missed cancer diagnoses.

A practical solution to mitigate this issue is the integration of an automated alert system into pathology reporting. Pathologists could activate a warning for unexpected malignant findings, thereby drawing clinicians' attention to critical results. This straightforward intervention has the potential to significantly reduce missed diagnoses, facilitating timely management and ultimately improving patient outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was reviewed and approved by Hitit University Non-interventional Clinical Researches Ethics Committee (Date: 15.10.2024, Decision No: 2024-107).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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